

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claims 1-61 (canceled)

Claim 62 (currently amended) A method for producing a non-human transgenic animal, ~~said-the~~ method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of ~~said-the~~ somatic cell to a recipient cell to produce a nuclear transfer unit;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother; and
- (e) ~~(e)~~ causing-allowing ~~said-the~~ animal embryo to develop to term, thereby producing a non-human transgenic animal.

Claim 63 (currently amended) The method of claim 62, wherein ~~said-the~~ transgenic animal is a transgenic sheep, cow, bull, goat, pig, horse, camel, rabbit or rodent.

Claim 64 (currently amended) The method of claim 62, wherein ~~said-the~~ genetic targeting event is mediated by homologous recombination.

Claim 65 (currently amended) The method of claim 62, wherein ~~said-the~~ genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

Claim 66 (currently amended) The method of claim 62, wherein ~~said-the~~ genetic targeting event results in inactivation of a gene.

Claim 67 (currently amended) The method of claim 62, wherein ~~said the~~ genetic targeting event results in a gene targeted cell clone: randomly targeted cell clone ratio of equal to or greater than 1:100.

Claim 68 (canceled)

Claim 69 (canceled)

Claim 70 (currently amended) The method of claim 62, wherein ~~said the~~ modification comprises placing a promoter adjacent to an endogenous gene in the nuclear genome.

Claim 71 (currently amended) The method of claim 70 ~~35 or 36~~, wherein ~~said the~~ promoter is a collagen gene promoter.

Claim 72 (currently amended) The method of claim ~~69 or~~ 70, wherein ~~said the~~ promoter is a milk protein gene promoter.

Claim 73 (currently amended) The method of claim ~~69 or~~ 70, wherein ~~said the~~ promoter directs abundant expression of at least one gene in fibroblast cells.

Claim 74 (canceled)

Claim 75 (currently amended) The method of claim 62, wherein ~~said the~~ modification comprises placing a marker gene at ~~said the~~ endogenous locus in ~~said the~~ nuclear genome.

Claim 76 (currently amended) The method of claim 75~~41~~, wherein ~~said the~~ marker gene is a gene that confers resistance to a drug.

Claim 77 (currently amended) The method of claim 76~~42~~, wherein ~~said the~~ gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.

Claim 78 (currently amended) The method of claim ~~7541~~, wherein ~~said the~~ marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

Claim 79 (currently amended) The method of claim ~~78~~[44], wherein ~~said the~~ visible marker gene is GFP.

Claim 80 (currently amended) The method of claim 62, wherein ~~said the~~ modification comprises removing a negatively selectable marker gene.

Claim 81 (currently amended) The method of claim ~~80~~ 46, wherein ~~said the~~ negatively selectable marker gene is a toxin gene.

Claim 82 (currently amended) The method of claim 62, wherein ~~said the~~ genetic targeting event is mediated by lipofection.

Claim 83 (currently amended) The method of claim 62, wherein ~~said the~~ genetic targeting event comprises the use of a gene targeting vector, which vector comprises a region of homology to a target locus.

Claim 84 (currently amended) The method of claim 83, wherein ~~said the~~ region of homology is greater than 7 kb in length.

Claim 85 (currently amended) The method of claim 62, wherein ~~said the~~ genetic targeting event comprises the use of a gene targeting vector which is in a circular form.

Claim 86 (currently amended) The method of claim 62, wherein ~~said the~~ somatic cell is a primary somatic cell.

Claim 87 (currently amended) The method of claim 62, wherein ~~said-the~~ somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

Claim 88 (currently amended) The method of claim 62, wherein ~~said-the~~ somatic cell is a G<sub>0</sub> cell.

Claim 89 (currently amended) The method of claim ~~88~~54, wherein ~~said-the~~ G<sub>0</sub> cell is obtained by serum starvation of a somatic cell.

Claim 90 (currently amended) A method for producing transgenic offspring from a transgenic animal, ~~said-the~~ method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of ~~said-the~~ somatic cell to a recipient cell;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother;
- (e)-(e) causing-allowing said-the animal embryo to develop to term, thereby producing a non-human transgenic animal; and.
- (d)(f) breeding ~~said-the~~ transgenic animal to produce transgenic offspring from ~~said-the~~ transgenic animal.

Claim 91 (new) A transgenic animal obtained by the method of claim 62.

Claim 92 (new) A transgenic animal obtained by the method of claim 90.

Claim 93 (new) The transgenic animal of claim 91 or 92 which is a sheep, cow, bull, goat, pig, horse, camel, rabbit or rodent.

Claim 94 (new) The transgenic animal of claim 91 or 92 which is a sheep.

Claim 95 (new) The transgenic animal of claim 91 or 92 which is a cow.

Claim 96 (new) The transgenic animal of claim 91 or 92 which is a pig.

Claim 97 (new) The method of claim 90, wherein the transgenic animal is a transgenic sheep, cow, bull, goat, pig, horse, camel, rabbit or rodent.

Claim 98 (new) The method of claim 90, wherein the genetic targeting event is mediated by homologous recombination.

Claim 99 (new) The method of claim 90, wherein the genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

Claim 100 (new) The method of claim 90, wherein the genetic targeting event results in inactivation of a gene.

Claim 101 (new) The method of claim 90, wherein the genetic targeting event results in a gene targeted cell clone: randomly targeted cell clone ratio of equal to or greater than 1:100.

Claim 102 (new) The method of claim 90, wherein the modification comprises placing a promoter adjacent to an endogenous gene in the nuclear genome.

Claim 103 (new) The method of claim 102, wherein the promoter is a collagen gene promoter.

Claim 104 (new) The method of claim 102, wherein the promoter is a milk protein gene promoter.

Claim 105 (new) The method of claim 102, wherein the promoter directs abundant expression of at least one gene in fibroblast cells.

Claim 106 (new) The method of claim 90, wherein the modification comprises placing a marker gene at the endogenous locus in the nuclear genome.

Claim 107 (new) The method of claim 106, wherein the marker gene is a gene that confers resistance to a drug.

Claim 108 (new) The method of claim 107, wherein the gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.

Claim 109 (new) The method of claim 106, wherein the marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

Claim 110 (new) The method of claim 109, wherein the visible marker gene is GFP.

Claim 111 (new) The method of claim 90, wherein the modification comprises removing a negatively selectable marker gene.

Claim 112 (new) The method of claim 111, wherein the negatively selectable marker gene is a toxin gene.

Claim 113 (new) The method of claim 90, wherein the genetic targeting event is mediated by lipofection.

Claim 114 (new) The method of claim 90, wherein the genetic targeting event comprises the use of a gene targeting vector, which vector comprises a region of homology to a target locus.

Claim 115 (new) The method of claim 114, wherein the region of homology is greater than 7 kb in length.

Claim 116 (new) The method of claim 90, wherein the genetic targeting event comprises the use of a gene targeting vector which is in a circular form.

Claim 117 (new) The method of claim 90, wherein the somatic cell is a primary somatic cell.

Claim 118 (new) The method of claim 90, wherein the somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

Claim 119 (new) The method of claim 90, wherein the somatic cell is a G<sub>0</sub> cell.

Claim 120 (new) The method of claim 119, wherein the G<sub>0</sub> cell is obtained by serum starvation of a somatic cell.

Claim 121 (new) The method of claim 62 or 90, wherein the genetic targeting event is mediated by electroporation.

Claim 122 (new) The method of claim 62 or 90, wherein the genetic targeting event is mediated by transfection.

Claim 123 (new) The method of claim 66, wherein the gene that is inactivated is  $\alpha$ -1,3 galactosyltransferase.

Claim 124 (new) The method of claim 99, wherein the gene that is inactivated is  $\alpha$ -1,3 galactosyltransferase.

Claim 125 (new) The method of claim 62 or 90, wherein the endogenous locus is an immunoglobulin gene.

Claim 126 (new) The method of claim 123, 124 or 125, wherein the transgenic animal is a pig.

Claim 127 (new) The method of claim 123, 124 or 125, wherein the transgenic animal is a cow.

Claim 128 (new) A transgenic pig obtained by the method of claim 123 or 124.

Claim 129 (new) A transgenic pig obtained by the method of claim 125.

Claim 130 (new) A transgenic cow obtained by the method of claim 125.

Claim 131 (new) A method for producing a non-human transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) accomplishing successful nuclear transfer to produce the non-human transgenic animal.

Claim 132 (new) A method for producing a non-human transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to an activated recipient cell to produce a nuclear transfer unit;
- (c) transferring the nuclear transfer unit to a surrogate mother; and
- (d) allowing the animal embryo to develop to term, thereby producing a non-human transgenic animal.



Claim 133 (new) A method for producing transgenic offspring from a transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to a recipient cell;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother;
- (e) allowing the animal embryo to mature in a manner that accomplishes breeding.